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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/457,421 | 12/07/1999 | ALAN A. DAVIS | AHP92038-2-C | 7663 |

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WYETH
PATENT LAW GROUP
5 GIRALDA FARMS
MADISON, NJ 07940

| EXAMINER | |
|---|---|
| LE, EMILY M | |
| ART UNIT | PAPER NUMBER |
| 1648 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/457,421 | DAVIS ET AL. | |
| | Examiner | Art Unit | |
| | Emily Le | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *31/06, 7/14/06, 8/25/06 and 12/11/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *26 and 28-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26 and 28-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Appeal*

1. In view of the appeal brief filed on 3/31/06, 7/14/06, 8/25/06 and 12/11/06, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

/Bruce R. Campell/
Bruce R. Campell
Supervisory Patent Examiner
Art Unit 1648

### *Status of Claims*

2. Claims 1-25 and 27 are cancelled. Claims 28 and 29-40 are pending and under examination.

***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 26, 29, 30, 31, 33, 35, 38-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chanda et al.,[1] in view of Chengalvala et al.[2] and Morin et al.[3]

The claims are directed to the administration of an immunogenic composition comprising a recombinant adenovirus comprising an expression cassette containing a promoter, a nucleic acid sequence encoding the HIV-1 gp160, the envelope glycoprotein antigen, to a human to induce an immure response against HIV-1 infection. The claims additionally require that the administration be followed with one or more intranasal or intramuscular booster administration of the recombinant adenovirus. Claim 29, which depends on claim 26, requires the adenovirus to be of serotype 4, 5 or 7. Claim 30, which depends on claim 26, requires the insertion of a rev gene along with the nucleic acid sequence encoding the HIV-1 gp160. Claim 31, which depends on claim 26, requires the HIV-1 gp160 be that of the MN or LAV strain. Claims 33 and 35, which depend on claim 26, require the intranasal dosage administered be about $1x10^7$pfu, and the booster dosage be in the range of $1x10^7$ to $1x10^8$ pfu, respectively.

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[1] Chanda et al. High level expression of envelope glycoproteins of the human immunodeficiency virus type I in presence of rev gene using helper-independent adenovirus type 7 recombinants. Virology, 1990, Vol. 175, 535-547.

[2] Chengalvala et al. Adenovirus Vectors for Gene Expression. Current Opinion in Biotechnology, October 1991, 2, 718-722.

Claims 38-40, which depend on claim 26, requires the adenovirus to comprise a deletion in the E3 region, both E1 and E3 regions, and E1 region.

Chanda et al. teaches an immunogenic composition comprising a recombinant adenovirus comprising an expression cassette containing a promoter, a nucleic acid sequence encoding the HIV-1 gp160, the envelope glycoprotein antigen, and REV polypeptide sequence and a polyadenylation signal sequence. The adenovirus used by Chanda et al. is serotype 7, comprises a deletion in the E3 region, and the HIV-1 gp160 sequence used by Chanda et al. is the LAV strain gp160 sequence. [Figure 1, in particular.] Chanda et al. teaches that the composition is an excellent source of HIV-1 envelope antigen, which is capable of inducing protective immunity against HIV and are known to induce a good cell mediated immune response as well as cytotoxic T cell activity; and suggests the use of the composition as a candidate vaccine against HIV-1 infection. [Last sentence, paragraph bridging pages 544-545, and Introduction section, page 535-536, in particular.]

As noted, Chanda et al. teaches a deletion of the E3 region in the adenovirus, and does not teach a deletion in the E1 region. However, with a deletion in just the E3 region, Chanda et al. recognizes the packaging difficulties encountered with this sole deletion. And, at the time the invention was made, Chengalvala et al. teaches the deletion of the E1 region to permit packaging of larger gene inserts. Hence, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to also delete the E1 region of the composition of Chanda et al. One of

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[3] Morin et al. Recombinant Adenovirus Induces Antibody Response to Hepatitis B virus Surface Antigen

ordinary skill in the art, at the time the invention was made, would have been motivated to do so to enable packaging of larger gene inserts. One of ordinary skill in the art, at the time the invention was made, would have a reasonable expectation of success for doing so because deletion of the E1 region to permit packaging of larger genes is routinely practiced in the art.

While Chanda et al. does suggest the use of the composition as a candidate vaccine against HIV-1 infection, Chanda et al. does not teach the administration of the immunogenic composition. However, at the time the invention was made, Chengalvala et al. also teaches the administration of an immunogenic composition comprising a recombinant adenovirus using the booster administration regimen to substantially enhance the immune response induced by the envelope glycoprotein antigen. [First full paragraph, left column, page 720, in particular.] Thus, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to administer the immunogenic composition of Chanda et al. using a booster administration regimen. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to enhance the immune response induced by the immunogenic composition of Chanda et al. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the use of booster regimen is routinely practiced in the art.

It is noted that Chengalvala et al. did not intranasally administer the composition comprising a recombinant adenovirus, however, at the time the invention was made,

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in Hamsters. Proc. Natl. Acad. Sci. USA, July 1987, Vol. 84, 4626-4630.

Morin et al. establishes that intranasal administration is an acceptable form of administration for an immunogenic composition comprising a recombinant adenovirus. The intranasal dosage taught by Morin et al. is $1x10^7$ and $1X10^8$ pfu, which is about $1x10^7$ and in the range of $1x10^7$ to $2x10^9$ pfu. [Table 1, page 4629, in particular.] Thus, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to intranasally administer the immunogenic composition of Chanda et al. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to facilitate the delivery of the immunogenic composition. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because intranasal administration of the immunogenic composition is an acceptable method of administration routinely practiced in the art.

Lastly, Chanda et al., Chengalvala et al. and Morin et al. do not teach the administration of the composition to a human. However, at the time the invention was made, it would have been prima facie obvious to one of ordinary skill in the art to administer the immunogenic composition of Chanda et al. to a human. One of ordinary skill in the art would have been motivated to do so to induce a cell mediated immune response as well as cytotoxic T cell activity against HIV. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the composition of Chanda et al. is expected to retain its immunogenic properties regardless of the patient population.

5. Claims 26 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chanda et al., in view of Chengalvala et al. and Morin et al., as applied to claim 26, in further view of Vernon et al.[4]

Claim 32, which depends on claim 26, requires the immunogenic composition comprising a recombinant adenovirus comprising an expression cassette containing a promoter, a nucleic acid sequence encoding the HIV-1 gp160, the envelope glycoprotein antigen, and a polyadenylation signal sequence to be an immunogenic composition comprising a recombinant adenovirus comprising an expression cassette containing a promoter, a nucleic acid sequence encoding the gag-pro region of HIV-1, and a polyadenylation signal sequence.

The significance of Chanda et al., Chengalvala et al. and Morin et al., as applied to claim 26, is provided above.

As discussed above, Chanda et al. teaches an the immunogenic composition comprising a recombinant adenovirus comprising an expression cassette containing a promoter, a nucleic acid sequence encoding the HIV-1 gp160, the envelope glycoprotein antigen, and a polyadenylation signal sequence. The immunogenic composition of Chanda et al. does not comprise a recombinant adenovirus comprising an expression cassette containing a promoter, a nucleic acid sequence encoding the gag-pro region of HIV-1. However, Vernon et al. teaches an immunogenic composition comprising a recombinant adenovirus comprising an expression cassette containing a promoter, a nucleic acid sequence encoding the gag-pro region of HIV-1, and a

[4] Vernon et al. Ultrastructural characterization of human immunodeficiency virus type 1 gag-containing

polyadenylation signal sequence [Abstract, in particular]. Vernon et al. teaches that the immunogenic composition forms Gag antigen-containing, non infectious virus like particles. Vernon et al. suggests the use of the particles as an antigen bearing vehicles in vaccines against HIV. [Last complete paragraph, right column, page 1243, in particular.] Hence, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to use the immunogenic composition of Vernon et al. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to induce an immune response against HIV. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the composition of Vernon et al. is immunogenic.

6. Claims 26, 34 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chanda et al., in view of Chengalvala et al., as applied to claim 26, in further view of Quantin et al.[5]

Claims 34 and 36, which depend on claim 26, require the intramuscular dosage administered be in the range of $1x10^7$ to $2x10^9$ pfu, and the intramuscular booster dosage be in the range of $1x10^{10}$ to $8x10^{10}$ pfu, respectively.

The significance of Chanda et al. and Chengalvala et al., as applied to claim 26, is provided above. Neither Chanda et al. nor Chengalvala et al. teaches the intramuscular administration of the immunogenic composition.

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particles assembled in a recombinant adenovirus vector system. Journal of General Virology, June 1991, Vol. 72, 1243-1251.

[5] Quantin et al. Adenovirus as an expression vector in muscle cells in vivo. Proc. Natl. Acad Sci. USA, April 1992, Vol. 89, 2581-2584.

However, at the time the invention was made, Quantin et al. teaches that an immunogenic composition comprising a recombinant adenovirus is able to direct expression of antigens in muscle cells. Quantin et al. teaches the injection of the immunogenic composition, which comprises $10^8$ pfu, which is in the range of $1x10^7$ to $2x10^9$ pfu of the recombinant adenovirus into the thighs of mice. In the instant case, while it is not readily apparent that the injection type used by Quantin et al. is an intramuscular injection, it can readily be deduced that the injection is intramuscular because Quantin et al. has expressed his interest in evaluating the ability of immunogenic composition comprising a recombinant adenovirus to direct expression of antigens in muscle cells. Additionally, in the event that this is not readily apparent to Applicant, it remains that Quantin et al. suggests intramuscular injections as a suitable form of delivery for immunogenic composition comprising a recombinant adenovirus since Quantin et al. teaches that the immunogenic composition is able to direct expression of antigens in muscle cells.

Hence, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to administer the immunogenic composition of Chanda et al. intramuscularly. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to facilitate delivery of the immunogenic composition. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the immunogenic composition comprising recombinant adenovirus is cable of directing expression of antigens in muscle cells.

Additionally, it is noted that Chanda et al., Chengalvala et al. and Quantin et al. do not teach an intramuscular booster dosage in the range of $1x10^{10}$ to $8x10^{10}$ pfu. However, it would have been prima facie obvious for one of ordinary skill in the art, at the time the invention was made to optimize the intramuscular dosage amount. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to optimize the immune response induced by the immunogenic composition of Chanda et al. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the determination of workable range or optimal range is routinely practiced in the art.

7. Claims 26-27 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chanda et al., in view of Chengalvala et al. and Morin et al., as applied to claim 26, in further view of Haigwood et al.[6]

Claim 27, which depends on claim 26, requires one or more intramuscular administration of an HIV-1 antigen polypeptide following the booster administration, wherein the antigen polypeptide is a gag polypeptide or an envelope polypeptide or combination thereof. Claim 37, which depends on claim 27, requires that intramuscular dosage of the antigen polypeptide be between 200 μg and .5mg, which equates to .2 mg to .5 mg.

The significance of Chanda et al. Chengalvala et al. and Morin et al., as applied to claim 26, is provided above. Chanda et al. Chengalvala et al. and Morin et al. do not teach the administration of an HIV-1 antigen polypeptide. However, it is noted that both

Chanda et al. and Chengalvala et al. are interested in the induction of an immune response against HIV with the use of the immunogenic composition comprising recombinant adenovirus to express the HIV-1 envelope glycoprotein antigen, which is a polypeptide, as a vaccine candidate against HIV. Chanda et al. also establishes the use of envelope polypeptide as a vaccine candidate against HIV. [Introduction, page 535, in particular.]

At the time the invention was made, Haigwood et al. teaches the intramuscular administration of a recombinant gp120 envelope polypeptide to induce an immune response against HIV. [Abstract, in particular.] Haigwood et al. teaches the use of an interrupted immunization schedule, which involves the use of booster administrations, wherein .055 mg of the gp120 envelope polypeptide were administered 9 times over a period of 81 weeks. [Immunization Protocols section, right column, page 173, in particular.] Thus, the total dosage intramuscular amount of gp120 envelope polypeptide administered by Haigwood et al. is .45 mg, which is between .2 mg to .5 mg. [A subunit dose of .55 mg administed 9 times equals .45 mg dose.] Hence, at the time the invention was made, the art teaches the administration of both an HIV-1 antigen polypeptide and immunogenic composition comprising a recombinant adenovirus encoding the HIV-1 gp160 envelope glycoprotein antigen to induce an immune response against HIV. Thus, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to combine the teachings of Haigwood et al. with that of Chanda et al., Chengalvala et al. and Morin et al. One of

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[6] Haigwood et al., Native but not denatured recombinant human immunodeficiency virus type 1 gp120

ordinary skill in the art, at the time the invention was made, would have been motivated to do so to optimize the immune response induced against HIV. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the art teaches the use of HIV antigens to induce immune response against HIV.

***Conclusion***

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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generates broad-spectrum neutralizing antibodies in baboons. Journal of Virology, January 1992, Vol. 66, No. 1, 172-182.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Emily M. Le/
Patent Examiner
Art Unit 1648

/E.Le/